

CALIFORNIA STATE DEPARTMENT OF PUBLIC HEALTH

WALTER M. DICKIE, M.D., Director

Weekly Bulletin



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GUY P. JONES
EDITOR

Coccidioidal Granuloma*

By HIRAM E. MILLER, M.D.

The first human infection of coccidioidal granuloma was observed by Posadas and Wernike¹ in Buenos Aires, in 1892. Rixford and Gilchrist² described the first California cases two years later. The causative organism was properly classified by Ophüls and Moffitt³ in 1900. Occurrence of the disease in animals has been known for a number of years⁴. The infecting organism was isolated from the soil by Stewart and Meyer⁵ in 1932. In the 43 years that have elapsed since the disease was first recognized, very little progress has been made in its treatment or prevention. Most of the remedies in use have been recommended by practitioners of medicine and not by trained medical investigators. California research institutes have more or less ignored this pressing local problem, partially due to lack of funds and the personal danger involved.

It is not necessary to review the epidemiology, symptomatology or therapy of coccidioidal granuloma in presenting this subject to this Health Officers' Section of the League of California Municipalities. You are all familiar with the disease, and the facts concerning it are so well given in the California Department of Public Health Bulletin No. 57 published in 1931.

* From the Division of Dermatology, University of California Medical School.
Read before the Health Officers' Section, League of California Municipalities, San Francisco, September 23, 1935.

As a clinician I am most interested in the prevention and cure of coccidioidal granuloma. The apparent heavy infestation of soil and vegetable matter in certain areas seems to preclude the possibility of destroying the causative organism at its source. There should, however, be some means of immunizing humans against it or some therapeutic procedure to arrest more than an occasional case.

COCCIDIOIDAL GRANULOMA IN CHILDREN

Of the 403⁶ reported cases of coccidioidal granuloma, 42, or about 10 per cent, are in children ranging from three months to 18 years of age. Prac-

CALIFORNIA CASES—COCCIDIOIDAL GRANULOMA

AGE	NUMBER OF CASES	PERCENTAGE
0-18 -----	42	10 %
18- -----	355	88.5%
Unknown -----	6	1.5%
TOTALS -----	403	100 %

tically all of these are Mexican or Filipino children who have been in the endemic areas for only a short period of time. It is perhaps remarkable that more children of parents with long residence in endemic areas do not develop the disease. Some of us have the opinion that children may acquire coccidioidal granuloma in a mild form from which they recover

and develop a resistance, and that this may prevent further symptoms throughout a lifetime. They may also have some inherited resistance built up through many generations. Coccidioidal granuloma may in this manner act in a similar way to tuberculosis.

We have a colored girl 11 years of age under our observation at the University Hospital. She has an orange-sized subcutaneous abscess of coccidioidal granuloma on her back with many scattered bone lesions. We are giving her small injections of tartar emetic twice a week, together with cod-liver oil, good food, etc. We will watch her progress with considerable interest to determine if she reacts to the infection in a different manner from adults. It would be of more interest if she were the child of a family with a long residence in an endemic area. A careful study of children in the San Joaquin Valley running a low-grade fever, would be of interest.

COCCIDIOIDAL GRANULOMA IN ADULTS

Coccidioidal granuloma occurs more frequently in recent arrivals to an endemic area than in older inhabitants. A survey of the reported cases in which length of residence is given shows that almost 40 per cent of the patients have been in the infected areas for one year or less, and many for only a few weeks. It is also of interest that only 28 per cent

CALIFORNIA CASES OF COCCIDIOIDAL GRANULOMA

NATIONALITY	NUMBER	PERCENTAGE
American -----	115	28%
Foreign-born -----	271	68%
Mexican -----	94	23 %
Filipino -----	57	14 %
Negro -----	48	12 %
Japanese -----	10	2½ %
Etc. -----	etc.	etc.
Unknown -----	17	4%
TOTALS -----	403	100%

of the 403 reported patients are listed as "Americans." The remaining 72 per cent are foreign-born. This percentage is not in accord with the number of foreign-born in the population of the endemic area. These findings suggest that the old inhabitants of endemic areas may possess some resistance or immunity to an infection with *coccidioides immitis*.

COCCIDIOIDAL GRANULOMA IN ANIMALS

Giltner in 1918 reported 1 case in cattle; Beck in 1929, 6 cases in cattle and 1 in sheep; Traun in 1929, 2 cases in cattle; and Beck in 1931, 10 cases in cattle.⁴ Only bronchial and mediastinal lymph-nodes were studied in these animals. There is no evidence of direct animal to man transmission of the disease.

Animals apparently have a marked resistance to the disease and do not die of it. Perhaps this resistance in animals may be made use of in therapy. There may be a possibility of increasing it by suitable inoculation to such a point that serum from the animal would be of therapeutic value in human infections.

FORMS OF COCCIDIOIDES ORGANISMS

Recent studies in Brazil have shown two additional types of coccidioidal granuloma:⁷ "*Pseudococcidioides mazzai*" and "*Paracoccidioides braziliensis*." The first reported case of pseudococcidioides was a laryngeal infection. Two hundred and fifty-seven cases of paracoccidioides have been reported from Brazil. De Almeida has shown peculiar chromatin masses at the periphery of the double-contoured organisms in this form of the disease. More thorough investigation of coccidioidal granuloma in the United States may show that the disease is caused by a group of molds, and not by a single species. It also may be found that the therapy effective in the disease due to one form of the organism may be useless when it is caused by another type.

Intensive study of coccidioidal granuloma is being carried on in South America. If friendly scientific rivalry exists between research institutes of the North and South American continents, this should stimulate and renew our interest in this disease.

INTRADERMAL TESTS

Davis⁹ in 1923 perfected an intradermal skin test with killed coccidioides organisms. The reaction was quite intense in a patient with a coccidioidal granuloma of 12 years' duration. This test has been used by many observers in recent years. A positive reaction is invariably obtained in patients with the disease. It would be of interest to carry out a series of these tests on a large group of children and adults in the San Joaquin Valley without evidence of a coccidioidal infection.

DISTRIBUTION

Between 85 and 90 per cent of the 403 reported cases of coccidioidal granuloma originated in the State of California. The 257 cases of paracoccidioides from Brazil are not included in these statistics. The remaining 10 to 15 per cent came from widely scattered areas. Cases have been reported from Italy, South America, Mexico, Alaska, Illinois, Nebraska, Texas, Tennessee, Louisiana, Washington, etc.

Of special interest are 2 cases recently reported from Hawaii.⁸ One was a pulmonary infection in a Filipino who had been in the San Joaquin Valley. The second patient was a full-blooded Hawaiian with

a lesion on one leg. He had never been away from the islands and did not come in contact with the previous patient.

ASSOCIATION WITH TUBERCULOSIS

Patients with both coccidioides and tuberculosis have been of interest to me. The terminal picture of many patients with pulmonary coccidioides is that of tuberculosis, with sputum laden with tubercle bacilli. Perhaps the tuberculosis, as in many wasting diseases, is simply a terminal infection. I have also observed patients with a quiescent coccidioides develop active pulmonary tuberculosis.

Two cattle reported by Beck⁴ gave definite intradermal tuberculin reactions, and at autopsy were found to be affected with coccidioides without any evidence of tuberculosis. Positive tuberculin reactions have also been observed in guinea pigs injected with coccidioides. An investigation of the interrelationship of these two diseases may prove to be of considerable interest.

TREATMENT

General treatment is probably of more value in coccidioidal granuloma than any specific remedy. Good food, rest, sunshine and general medical care, as used in tuberculosis, should be advised in all cases.

The amputation of an extremity when it alone seems to be involved may arrest the disease. This does not signify, however, that the infection is ever a local one. I have followed a patient for 12 years who has apparently remained free from all signs and symptoms of the disease after the amputation of a lower extremity. Characteristic double-contoured organisms can be obtained at any time from an insignificant dermatitis on his eyebrow.

Vaccines, X-ray, iodides, colloidal copper, antimony and potassium tartrate, etc., have apparently arrested or perhaps cured isolated cases. When given to other patients they do not seem to be of benefit. There is no remedy that will cure even a small percentage of patients.

In recent years we have attempted to give each patient with coccidioides who came under our care a remedy that had not, to our knowledge, previously been used in the treatment of coccidioidal granuloma. The results were not encouraging.

1. "*Fuadin*." When this drug was first introduced, we gave it to one patient without beneficial results.

2. *Antimony and potassium tartrate* in large doses. Ten c.c. of a 1 per cent solution were given intravenously every 3 days for 15 injections, without benefit. Five c.c. is the usual dose.

3. "*Atabrine*," an acridin derivative probably superior to quinine in the treatment of malaria, was given to 2 patients without improvement.

4. *Heat therapy*. One patient was given 6 treatments at weekly intervals, in which the body temperature was raised to 103-104° and kept there from 3 to 5 hours. An unrecognized associated tuberculosis of the kidney became active under this treatment. The coccidioidal granuloma was not improved.

5. *Pooled serum* from healthy adults living in Tulare County for long periods of time. Following the injection of 50 c.c. of this serum intramuscularly in one patient, most of the adult forms of the double-contoured organism developed many minute filaments extending out from the periphery of the capsule. These were observed for 3 days only, in all fresh specimens of pus examined.

Perhaps one or more of the individuals from whom the serum was obtained had recovered from a coccidioidal granuloma in childhood and had developed a resistance to the disease. Perhaps the changes in the organisms were simply coincidental. In any event, more serum was obtained from another group of adults in Tulare County and given to two patients without any changes in the organisms or improvement in the patients. The group from which this last serum was obtained may not have contained an individual with a resistance to the infection.

It would be of interest to obtain serum from a patient who had recovered from an infection with *coccidioides immitis* and give it to an early case. It is not known whether antibodies are developed to this type of infection. Further investigation of immunity and resistance in coccidioidal granuloma is necessary.

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(Continued in next issue)

MORBIDITY

Complete Reports for Following Diseases for Week Ending
January 4, 1936

Chickenpox

394 cases: Alameda 1, Albany 1, Berkeley 8, Oakland 18, San Leandro 1, Gridley 6, Colusa 1, Contra Costa County 5, Hercules 5, Pittsburg 3, El Dorado County 2, Placerville 2, Fresno County 4, Reedley 1, Eureka 1, Imperial County 2, Westmoreland 1, Kern County 4, Kings County 15, Los Angeles County 10, Alhambra 2, Burbank 2, Culver City 5, Glendale 6, Huntington Park 2, Los Angeles 47, Montebello 1, Pasadena 7, Santa Monica 1, Vernon 1, Whittier 2, South Gate 2, Monterey Park 2, Merced 2, King City 1, Monterey 1, Orange County 6, Orange 3, Santa Ana 14, Beaumont 4, Sacramento County 7, Sacramento 5, San Bernardino 6, Upland 1, San Diego County 36, Chula Vista 4, Escondido 8, National City 8, San Diego 36, San Francisco 35, San Joaquin County 12, Manteca 2, Stockton 2, Tracy 1, San Luis Obispo County 1, Menlo Park 2, Santa Barbara County 2, Santa Barbara 4, Santa Maria 1, Santa Clara County 1, San Jose 1, Santa Cruz County 2, Shasta County 2, Siskiyou County 1, Porterville 1, Ventura County 2, Santa Paula 1, Ventura 1, Yolo County 1, Woodland 6.

Diphtheria

44 cases: Alameda 2, Hayward 1, Oakland 3, Fresno 1, Imperial County 1, Kern County 1, Los Angeles 8, San Gabriel 2, Whittier 1, Monterey County 1, Napa County 1, Sacramento 2, Hollister 1, San Bernardino 1, San Diego County 3, San Diego 2, San Francisco 2, San Joaquin County 1, San Luis Obispo County 3, Santa Barbara 1, Sutter County 2, Santa Paula 2, Ventura 1, Yuba County 1.

German Measles

56 cases: Alameda County 1, Berkeley 3, Hayward 2, Oakland 3, Calaveras County 1, Contra Costa County 6, El Cerrito 2, Fresno County 4, Sanger 1, Humboldt County 1, Long Beach 4, Los Angeles 6, Pomona 1, South Pasadena 1, Monterey County 1, Monterey 1, Orange County 1, Anaheim 2, Santa Ana 2, Tustin 4, San Diego County 1, Chula Vista 3, San Diego 1, San Francisco 1, Santa Clara County 1, Palo Alto 1, Yolo County 1.

Influenza

63 cases: Berkeley 2, Contra Costa County 2, Kern County 2, Lake County 1, Los Angeles County 7, Alhambra 1, Burbank 1, Glendale 3, Los Angeles 27, Napa County 1, Grass Valley 1, Huntington Beach 1, Riverside County 1, Riverside 3, San Diego 1, San Francisco 6, South San Francisco 1, Stanislaus County 1, Ventura County 1.

Malaria

One case: San Joaquin County.

Measles

439 cases: Albany 4, Berkeley 17, Oakland 42, Butte County 34, Gridley 2, Colusa County 1, Contra Costa County 1, El Cerrito 1, Richmond 1, Fresno County 2, Fresno 2, Ferndale 1, Kern County 1, Los Angeles County 15, Beverly Hills 2, Glendale 1, Huntington Park 1, Long Beach 5, Los Angeles 56, Pasadena 11, Pomona 3, Santa Monica 1, South Pasadena 1, Madera 4, Fort Bragg 6, Alturas 4, Monterey County 33, Carmel 1, Monterey 2, Salinas 7, Orange County 2, Fullerton 2, Santa Ana 1, Riverside County 1, Riverside 1, Sacramento County 3, San Benito County 1, Upland 1, San Diego County 3, Escondido 2, National City 1, San Francisco 83, Stockton 1, San Luis Obispo County 2, San Luis Obispo 1, South San Francisco 6, Santa Barbara County 1, Lompoc 1, Santa Barbara 1, Santa Clara County 8, Gilroy 1, Mountain View 5, San Jose 2, Sunnyvale 8, Santa Cruz County 1, Ventura County 14, Fillmore 1, Ventura 2, Yolo County 15, Woodland 6.

Mumps

341 cases: Berkeley 1, Oakland 16, Colusa County 9, Colusa 2, Contra Costa County 1, Richmond 1, Fresno 2, Humboldt County 1, Eureka 1, Kern County 4, Lake County 1, Los Angeles County 16, Claremont 2, Culver City 1, Glendale 2, La Verne 2, Long Beach 8, Los Angeles 26, Pomona 1, San Fernando 1, Santa Monica 1, Monterey Park 1, Madera 1, Mariposa County 2, Fort Bragg 12, Merced County 1, Grass Valley 4, Santa Ana 6, Riverside County 2, Beaumont 4, Corona 19, Riverside 5, Sacramento County 4, Sacramento 17, Ontario 1, San Diego 1, San Francisco 2, San Joaquin County 18, Stockton 4, Paso Robles 1, San Luis Obispo 1, Santa Barbara 6, Redding 1, Siskiyou County 1, Dunsmuir 122, Stanislaus County 2, Red Bluff 2, Ventura County 1, Woodland 1.

Pneumonia (Lobar)

101 cases: Berkeley 1, Oakland 1, Fresno County 3, Fowler 1, Ferndale 1, Westmoreland 1, Bakersfield 1, Los Angeles County 11, Burbank 1, Long Beach 1, Los Angeles 35, Monrovia 2, Pomona 1, South Gate 1, Monterey Park 1, Modoc County 1, Napa County 1, Orange County 3, Anaheim 1, Orange 3, La Habra 1, Riverside County 2, Riverside 2, Sacramento County 1, Sacramento 2, San Bernardino 2, Upland 1, San Diego County 4, Escondido 1, San Francisco 9, San Joaquin County 1, San Luis Obispo County 1, Paso Robles 1, Ventura 1, Yolo County 1.

Scarlet Fever

333 cases: Alameda 1, Berkeley 2, Oakland 4, Chico 2, Gridley 1, Contra Costa County 2, Martinez 2, Richmond 3, El Dorado County 3, Placerville 2, Fresno County 4, Fresno 1, Reedley 1, Humboldt County 2, Arcata 2, Eureka 2, Imperial County 5, Kern County 3, Kings County 4, Los Angeles County 25, Alhambra 3, Burbank 2, Glendale 4, Hermosa 1, Huntington Park 1, La Verne 1, Long Beach 3, Los Angeles 42, Monrovia 1, Montebello 3, San Fernando 2, San Gabriel 2, Santa Monica 4, Whittier 1, Lynwood 2, South Gate 4, Bell 2, Sausalito 1, Merced County 1, Monterey 1, Nevada County 3, Grass Valley 4, Nevada City 3, Orange County 3, Huntington Beach 1, Santa Ana 1, Tustin 1, Plumas County 4, Riverside County 2, Riverside 2, Sacramento County 9, Sacramento 21, Ontario 1, Redlands 1, San Bernardino 4, Upland 2, San Diego County 19, Coronado 2, La Mesa 1, National City 2, San Diego 13, San Francisco 32, San Joaquin County 2, Lodi 1, Stockton 4, Paso Robles 1, San Mateo County 1, Menlo Park 1, Lompoc 1, Santa Barbara 3, Santa Maria 1, San Jose 1, Willow Glen 2, Siskiyou County 4, Etna 1, Vallejo 1, Stanislaus County 1, Modesto 2, Oakdale 1, Turlock 2, Sutter County 2, Yuba City 2, Tehama County 1, Lindsay 2, Tulare 1, Ventura County 4, Ventura 1, Yolo County 1, Davis 2, Woodland 1, Yuba County 1, Marysville 1, California 1.*

Smallpox

3 cases: Los Angeles 1, Monterey County 2.

Typhoid Fever

8 cases: Los Angeles County 2, Los Angeles 1, Pomona 1, Riverside County 1, San Francisco 2, Stanislaus County 1.

Whooping Cough

109 cases: Alameda 1, Berkeley 1, Oakland 5, Fresno County 1, Fresno 1, Kern County 5, Kings County 1, Los Angeles County 16, Beverly Hills 2, Huntington Park 1, Long Beach 1, Los Angeles 22, South Gate 1, Maywood 1, Grass Valley 4, Fullerton 3, Santa Ana 1, Riverside 1, Sacramento 2, San Diego County 2, San Diego 13, San Francisco 8, San Joaquin County 2, Stockton 1, Tracy 2, San Luis Obispo County 3, Paso Robles 4, San Mateo 1, Watsonville 2, Ventura 1.

Meningitis (Epidemic)

9 cases: Los Angeles 7, San Diego County 1, Watsonville 1.

Dysentery (Amoebic)

3 cases: San Diego County 1, San Francisco 2.

Leprosy

2 cases: National City 1, California 1.*

Ophthalmia Neonatorum

One case: Brawley.

Pellagra

One case: San Francisco.

Poliomyelitis

7 cases: Reedley 1, Los Angeles 4, San Diego County 1, Daly City 1.

Tetanus

2 cases: Los Angeles 1, Anaheim 1.

Trachoma

2 cases: National City.

Encephalitis (Epidemic)

3 cases: Modoc County 1, San Diego County 2.

Paratyphoid Fever

One case: Santa Paula.

Trichinosis

2 cases: San Francisco.

Food Poisoning

3 cases: Pacific Grove 2, San Francisco 1.

Septic Sore Throat (Epidemic)

4 cases: Contra Costa County 1, San Diego 1, Daly City 1, South San Francisco 1.

Rabies (Animal)

21 cases: Calexico 3, Compton 1, Los Angeles 11, South Gate 2, San Diego County 2, National City 1, Stockton 1.

* Cases charged to "California" represent patients ill before entering the state or those who contracted their illness traveling about the state throughout the incubation period of the disease. These cases are not chargeable to any one locality.

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